The predictive value of the Patient Health Questionnaire-9 score for measuring the severity of coronary artery disease

Depression score and coronary artery disease

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Abstract

Aim: It is known that the prevalence of depression increases in patients with coronary artery disease (CAD). However, it is not clear whether patients' symptoms of depression worsen as the severity of CAD increases. The aim of this study is to investigate whether there is a relationship between the Patient Health Questionnaire-9 (PHQ) score and the severity of CAD.

Material and Methods: A total of 168 patients, diagnosed with stable and unstable angina, acute myocardial infarction, were included in the study. The patients were divided into two groups as mild (n=133) and severe CAD (n=35) according to the SYNTAX score (SS) results. All patients completed PHQ-9 questionnaires, reflecting their mood up to 2 weeks before the heart attack. Patients with a previous diagnosis of depression, coronary artery disease, using psychiatric drugs, severe heart and kidney failure were excluded from the study.

Results: The PHQ-9 score was higher in severe CAD (6.7±4.5 vs 12.5±15.0 p<0.000). Correlation analyses showed a strong association between PHQ-9 and SS (r=0.724, p<0.000) and heart rate (r=0.381, p<0.000). However, regression analysis showed that only SS [OR: 7.8, 95% CI (0.214-0.358), p<0.000] significantly increased the risk of depression. Receiver operating characteristics curve analyses presented that the optimal cut-off PHQ-9 score was ≥ 8 with 71.4 % sensitivity, 68.4 % specificity, and the area under the curve of 0.79, p < 0.000.

Discussion: PHQ-9 was higher in patients with severe CAD, and there was a strong link between PHQ-9 score and heart rate.

Keywords

Coronary artery disease; Patient health questionnaire; Depression

Introduction

The prevalence of depression is almost twice in patients with coronary artery disease (CAD) compared to the general population [1]. A sedentary life, smoking, alcohol consumption, stressful personality, which are among the risk factors for coronary artery disease, increase the tendency to depression. Conversely, depressed people have a stressful lifestyle that leads to more smoking, alcohol consumption, and CAD. It is known that compliance with medical treatment is poor in depressed patients and associated with unfavorable cardiovascular outcomes [2,3]. Therefore, the American Heart Association recommends routine screening for depression in patients with CAD and the European Society of Cardiology recommends the assessment of psychosocial risk factors with standardized questionnaires or clinical interviews in patients with CAD [4,5]. The Patient Health Questionnaire-9 (PHQ-9) scoring system is one of the approved questionnaires developed in the Diagnostic and Statistical Manual of Mental Disorders (DSM V) criteria for the diagnosis of depression in patients with coronary artery disease. This scoring is based on the patient's symptoms in the past 2 weeks. Each question is scored between 0 and 3, and if the total score is 10 or more, it can be considered depression [6]. To measure the severity of CAD, a different scoring system was developed. The SYNTAX score (SS) defines coronary artery dominance, lesion severity, the complexity, and the location. The SS is also used to predict cardiac outcomes after percutaneous coronary intervention (PCI) [7].

The aim of this study is to investigate whether there is a relationship between the PHQ score and the severity of CAD.

Material and Methods

A total of 168 patients diagnosed with stable and unstable angina, acute myocardial infarction were included in the study. BMI was calculated by taking height, weight, and waist circumference was measured from the midpoint of the distance between the archus costarum and the spina iliaca anterior superior. Biochemical and hematological blood parameters were obtained from the medical records of the patients. SS was calculated by monitoring angiography images. The patients were interviewed and informed about the PHQ-9 questionnaire, and completed the questionnaires themselves. The questionnaires were completed before the patient was discharged from the hospital.

SYNTAX score and Severity of CAD

Coronary angiographies (CAG) were performed using the Judkins technique, and all lesions ≥ 1.5 mm in diameter and causing 50 % stenosis in the coronary artery were included in the SS calculation [8]. After CAG, website software (http://www.SYNTAXscore.com) was used for the calculation of SYNTAX score. The SYNTAX score was calculated for following points: Coronary dominance, number of lesions, segment per lesion, total occlusion, bifurcation, trifurcation, aortic-osteal lesion, severe tortuosity, calcification, thrombus, diffuse/small vessel disease and lesion length > 20 mm. SS was calculated separately by two interventional cardiologists who did not know the study protocol and patient characteristics. Patients were divided into two groups according to SYNTAX scores as severe CAD (> 23) and mild CAD (≥ 22) [9].

Exclusion criteria

Patients with severe aortic and mitral valve stenosis, permanent cardiac pacemaker, advanced heart failure, chronic kidney failure, previous myocardial infarction, and patients having the psychiatric disease were excluded from the study.

PHQ-9 questionnaire

This survey is a depression component of the Patient Health Questionnaire developed according to the diagnostic criteria for major depressive disorders (DSM-V) [9,10]. PHQ -9 is a self-reporting tool that can help an intense clinician easily scan, diagnose, monitor, and correctly measure the severity of depression [10].

PHQ -9 is a survey that includes 9 questions, evaluating the symptoms of depression during the last two weeks. The time required to complete the questionnaire is usually 3-5 minutes. Each question is answered with one of four possible numbers between 0-3 (0 = Not at all, 1 = Several days, 2 = More than half of days, and 3 = Almost every day). Total scores in PHQ-9 can range from 0 to 27[10]' scoring: 1 to 4 points = minimal depression, 5 to 9 points = mild depression, 10 to 14 points = moderate depression, 15 to 19 points = moderately severe depression, 20 to 27 points = severe depression. A score of 10 or higher suggests possible depression and indicates the need for further investigation [10,11].

Statistical analysis

Statistical analysis was performed using SPSS 20.0 (IBM Corporation, Armonk, NY, USA). The baseline characteristics of the CAD patients were compared using Student's t-test for continuous variables, and the x2 Pearson's test was used for categorical variables. Pearson's correlation coefficient (r) and multivariable regression analyses were used to evaluate the strength of the relation between PHQ-9 score, SYNTAX score and heart rate. Then the receiver operating characteristics curve analysis (ROC) was used to evaluate the optimal cut-off the PHQ-9 score prediction model for high SS was applied to identify the optimal cut-off point. For all statistics, a p-value below 0.05 was considered significant.

Ethics Committee approval (decision no: YDU/2019/69-836, date: 30.05.2019) was obtained from the Non-Interventional Clinical Research Ethics Committee of Near East University, before the initiation of the study. The Declaration of Helsinki was followed in the application of ethical rules of the study. All subjects gave informed consent for participation.

Results

A total of 168 patients who were diagnosed with CAD by coronary angiography and who responded to the PHQ-9 questionnaire were included in the study. Thirty-five of these patients were severe CAD [mean age 59.3±11.2 years, 56 (81.2%) were males] and 133 of them were mild CAD [mean age 61.5±13.1 years, 75 (75.8%) were males].

There was no significant difference between LSS and HSS patients in terms of age, BMI, gender, waist circumference, systolic blood pressure, diastolic blood pressure, smoking and alcohol use, family history, before CAD history, ejection fraction values and medical treatment (p>0.05) (Table 1).

There was a significant difference in terms of PHQ-9 score (6.7 ± 4.5 vs 12.5 ± 5.2, p<0.000). However, serum creatinine

Table 1. Comparison of demographic features and medical history of patients with mild and severe CAD

Variables	Mild CAD (n=133)	Severe (n=35)	p-value
Age (years)	59.3±11.2	61.5±13.1	0.257
Gender (male %)	56 (81.2)	75 (75.8)	0.406
BMI (kg/m2)	30.1±5.8	28.9±5.4	0.185
Waist circumference (cm)	107.9±12.8	106.9±16.3	0.687
SBP (mmHg)	132.7±12.9	128.1±21.7	0.113
DBP (mmHg)	77.4±7.6	77.2±12.9	0.895
Heart rate (bpm)	80.8±13.2	82.1±17.5	0.593
Smoker (%)	22 (31.9)	39 (39.4)	0.319
Alcohol (%)	16 (23.2)	17 (17.2)	0.334
Hypertension (%)	33 (47.8)	51 (51.5)	0.638
Diabetes Mellitus (%)	18 (26.1)	33 (33.3)	0.315
Family History (%)	16 (23.2)	14 (14.1)	0.312
Before CAD (%)	20 (29.0)	26 (26.3)	0.637
Ejection Fraction (%)	52.5±10.6	53.4±9.8	0.850
Aspirin users (%)	18 (26.1)	23 (23.2)	0.637
B- blocker users (%)	22 (31.9)	21 (21.2)	0.119
Statin users (%)	14 (20.3)	20 (20.2)	0.987
CCB users (%)	6 (8.7)	14 (14.1)	0.284
ACEI users (%)	8 (11.6)	10 (10.1)	0.758
ARB users (%)	14 (20.3)	16 (16.2)	0.492

Abbreviations: ACEI: Angiotensin-converting enzyme inhibitors, ARB: Angiotensin II receptor blockers, BMI: Body mass index; CAD: Coronary artery disease, CCB: Calcium channel blocker, DBP: Diastolic blood pressure, SBP: Systolic blood pressure.

Table 2. Comparison of biochemical parameters PHQ-9 score in patients with mild and severe CAD

Variables	Mild CAD (n=133)	Severe CAD (n=35)	p-value
PHQ-9 score	6.7 ± 4.5	12.5±5.0	<0.000
Creatinine (mg/dL)	0.8±0.1	0.8±0.3	0.301
ALT (U/L)	27.0±16.0	33.7±59	0.356
AST (U/L)	24.7±11.6	27.6±12.9	0.430
Vitamin D (ng/mL)	19.8±23.0	18.1±12.0	0.567
Vitamin B 12 (pg/mL)	419.7±197 .4	361.3±193.2	0.195
Total cholesterol (mg/dL)	200.6±48.8	187.0±41.4	0.078
LDL-C (mg/dL)	125.2±29.0	121.7±34.0	0.426
HDL-C (mg/dL)	43.6±15.1	40.9±14.0	0.236
Triglyceride (mg/dL)	173.0±153.6	167.0±113.0	0.078
Glucose (mg/dL)	133.1±65.1	132.7±69.9	0.973
HbA1C (%)	6.1±1.4	6.3±1.5	0.436
Wbc (x103/uL)	8.6±2.0	8.7±3.1	0.512
Hb (g/dL)	13.7±1.8	13.2±1.8	0.122
PLT (x103/uL)	244.8±61.5	242.3±64.1	0.806
TSH (mIU/L)	1.6±1.0	1.7±1.4	0.402

Abbreviations: ALT: Alanine Transaminase, AST: Aspartate Aminotransferase, HR, Heart rate, Hb, Hemoglobin, HbA1c: Hemoglobin, HDL: High-density lipoprotein, LDL: Low-density lipoprotein cholesterol, n: number of patients, TSH, Thyroid stimulant hormone; WBC: White blood cell, PLT: Platelet.

Table 3. Multivariable logistic regression analyses between PHQ-9 score and SYNTAX score, heart rate and age

| Variables | Multivariable Regression analyses | | |
	OR	%95 CI (Lower Limit – Upper limit)	p-value
SYNTAX score	7.882	0.214 - 0.358	<0.000
Heart rate (bpm)	1.362	0.011 - 0.107	0.175
Age (year)	-0.703	0.073 - 0.308	0.483
Gender (female)	0.133	0.065-0.138	0.340

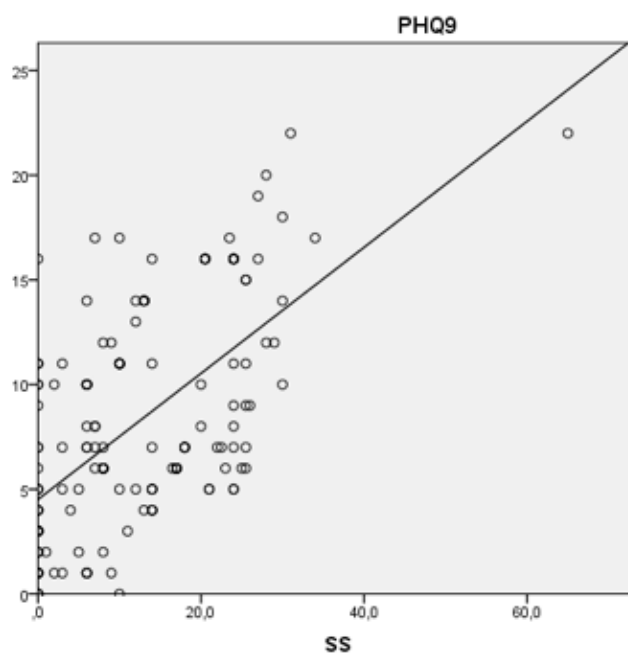Abbreviations: BMI, Body mass index.

Figure 1. Diagrams showing the association between PHQ-9 score and SYNTAX Score
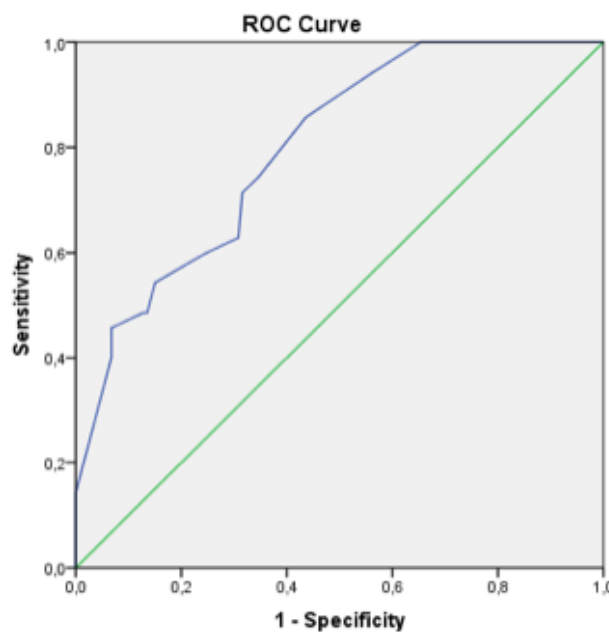

Figure 2. The ROC curve for PHQ-9 score to predict the coronary artery severity, AUC = 0.79 (95% CI 0.723–0.874, p < 0.000), with a sensitivity of 71.4 % and a specificity of 68.4 %.

levels (0.8±0.1 vs 0.8±0.3 mg/dl, p=0.301), serum aspartate transaminase (24.7±11.6 vs 54.6±82.9 U/L, p=0.003), alanine transaminase (27.0 ± 16.0 vs 33.7± 59.0 U/L, p=0.356), vitamin D (19.8 ± 23.0 vs 18.1 ± 12.1 ng/ml, p=0.567), vitamin B12 (419.7 ± 197.4 vs 361.3 ± 193.2 pg/ml, p=0.195), total cholesterol (200.6 ± 48.8 vs 187.0 ± 41.4 mg/dl, p=0.088), LDL (125.2 ± 29.0 vs 121.7 ± 34.0 mg/dl, p=0.426), triglycerides (173.0 ± 153.6 vs 167.0 ± 113.0 mg/dl, p=0.078), HDL(43.6 ± 15.1 vs 40.9 ± 14.0 mg/dl, p=0.236), glucose (133.1 ± 65.1 vs 132.7 ± 69.9 mg/dl, p=0.973), HbA1c (6.1 ± 1.4 vs 6.3 ± 1.5, p=436), thyroid-stimulating hormone (1.6 ± 1.0 vs 1.7 ± 1.4 mIU/L, p=0.402), serum hemoglobin (13.7 ± 1.8 vs 13.2 ± 1.8 g/dl, p=0.122), platelet levels (244.8 ± 61.5 vs 242.3 ± 64.1 x103

u/L, p=0.806), white blood cells (8.6±2.0 vs 8.7±3.1 x103 u/L, p=0.512) levels were similarly in two groups (Table 2).

Correlation analyses showed a strong association between PHQ-9 score and SS (r = 0.724, p < 0.000) and heart rate (r = 0.381, p < 0.000) (Figure 1).

Multivariable regression analysis showed that only SS [OR: 7.8, 95 % CI (0.214 - 0.358), (p<0.000)] were an independent risk factor for depression. No association was found between heart rate [OR: 1.3, 95 % CI (0.011-0.107), p=0.175], age [OR: -0.7, 95 % CI (0.073-0.308), p=0.483], and gender [OR: 0.1, 95 % CI (0.065-0.138), p=0.340] and PHQ-9 score (Table 3).

The ROC curve for PHQ-9 score to predict the coronary artery severity showed AUC = 0.79 (95% CI 0.723–0.874, p < 0.000), cut-off value was PHQ-9 = 8, with sensitivity 71.4 % and specificity 68.4 % (Figure 2).

Discussion

In our study, we found that the PHQ-9 score was higher in severe CAD, and there was a strong link between the PHQ-9 score and heart rate. To our knowledge so far, have not encountered a study on any link between severity of CAD and PHQ-9 questionnaire.

The pathophysiological process between depression and CAD begins with a change in the hypothalamic-pituitary gland axis and an increase in endocrine and inflammatory markers (C-reactive protein, interleukin-6, intercellular adhesion molecule-1 and increased fibrinogen). Changes in autonomic functions (activation of the sympathetic system and suppression of the activity of the parasympathetic system), leads to impaired endothelial and myocardial functions and the onset of hemostatic, inflammatory processes [12,13]. Increased catecholamines can also cause platelet activation with a procoagulant effect. Depression may increase coronary events both by accelerating the atherosclerotic process and by predisposition to thrombus. In our study, we found that patients with coronary artery disease had depressive symptoms 2 weeks before diagnosis, and patients with higher PHQ-9 scores had a higher severity of coronary artery stenosis.

Patient Health Questionnaire-9 (PHQ-9) is a nine-item questionnaire designed to identify depression in primary care and other medical settings. It has been shown in previous studies that the most appropriate method for diagnosing depression in coronary artery patients is the PHQ-9 score [14]. The PHQ-9 questionnaire standard cutoff score of 10 or greater maximizes the combined sensitivity and specificity for general and subgroups [15]. The strength of the PHQ-9 scores to predict depression in CAD has been tested in many studies. Haddad et al. in their study found that cut- points of PHQ-9 at ≥ 8 provide optimal test characteristics in CAD populations: a combination of test values (sensitivity = 94%; specificity = 84%; Youden Index 0.78), supports the selection of this breakpoint [14]. In our study, we found that a PHQ-9 score of ≥ 8 was significant for severe CAD.

Our study was a single-center, retrospective and subjectively conducted study based on the responses of patients to the PHQ-9 questionnaire. The number of patients was limited because we were able to enroll patients participating with their consent. In future studies, we believe that the relationship

between depression and severity of CAD can be examined in different populations and scoring systems. Since such a study has not been conducted before, it was difficult to reflect the differences in our study and make comparisons.

Impact statement

In our study, we found that the PHQ-9 score was higher in patients having serious CAD. Therefore, we believe it is important to explore patients with high SS for the likelihood of depression.

Conclusion

Depression is a general problem associated with high mortality and reduced quality of life in patients with CAD. Depression complicates the treatment of CAD by worsening cardiovascular risk factors, decreasing compliance with treatment and reducing adherence to a healthy lifestyle. In our study, we found that depression increased in patients with severe coronary artery disease. Therefore, in severe CAD, depression should be thoroughly investigated and treated.

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